IN THE CLAIMS

Please amend the claims as follows:

1. (Currently Amended) An *in vivo* assay system for determining the effect of a pharmaceutically acceptable compound on angiogenesis comprising:

a. A composition of microvascular endothelial cells; and

b. A non-human, immuno-compromised host,

wherein said cells have a recombinant expression cassette encoding telomerase, and wherein said compound modulates the formation of functional microvessels from said cells that communicate with the circulatory system of said host.

2. (Previously Presented) The *in vivo* assay system of claim 1 further comprising a digital imaging device.

3. (Previously Presented) The *in vivo* assay system of claim 2 wherein said device detects fluorescence.

4. (Previously Presented) The *in vivo* assay system of claim 1 wherein said cells stably express a transformed genetic marker.

5. (Previously Presented) The *in vivo* assay system of claim 4 wherein said transformed genetic marker is enhanced green fluorescent protein (eGFP).

6. (Previously Presented) The *in vivo* assay system of claim 1 wherein said cells are human dermal microvascular endothelial cells.

7. (Previously Presented) The *in vivo* assay system of claim 1 wherein said telomerase is a human telomerase reverse transcriptase catalytic subunit.

8. (Previously Presented) The *in vivo* assay system of claim 1 wherein said host is a SCID mouse.

9. (Previously Presented) The *in vivo* assay system of claim 1 wherein said compound is selected from the group consisting of growth factors, extracellular matrix molecules, proteinase inhibitors, cell adhesion molecules, angiostatic factors, apoptotic inducers, and inflammatory mediators.

10. (Previously Presented) The *in vivo* assay system of claim 9 wherein said compound is a growth factor.

11. (Previously Presented) The *in vivo* assay system of claim 10 wherein said growth factor is selected from the group consisting of angiopoietins, CTGF, EGF, FGF-2, IGF, PLGF, PDGF, SF, TGF, and VEGF.

12. (Previously Presented) The *in vivo* assay system of claim 11 wherein said growth factor is VEGF.

13. (Previously Presented) The *in vivo* assay system of claim 11 wherein said growth factor is FGF-2.

14. (Previously Presented) The *in vivo* assay system of claim 1 wherein said compound modulates tumor angiogenesis.

15. (Currently Amended) An *in vivo* method for analyzing the effect of a pharmaceutically acceptable compound on angiogenesis comprising:

a. providing a composition of microvascular endothelial cells, wherein said cells have a recombinant expression cassette encoding telomerase and a stably transformed genetic marker;

b. adding a compound that modulates the formation of functional microvessels to said cells to form a graft;

c. implanting said graft in a non-human, immuno-compromised host; and

d. determining the amount of neovascularization in said graft by measuring the expression of said transformed genetic marker.

16. (Previously Presented) The *in vivo* method of claim 15 wherein said cells are human dermal microvascular endothelial cells.

17. (Previously Presented) The *in vivo* method of claim 15 wherein said telomerase is a human telomerase reverse transcriptase catalytic subunit.

18. (Previously Presented) The *in vivo* method of claim 15 wherein said transformed genetic marker is enhanced green fluorescent protein (eGFP).

19. (Previously Presented) The *in vivo* method of claim 15 wherein expression of said transformed genetic marker is detected by a digital imaging device.

20. (Previously Presented) The *in vivo* method of claim 15 wherein said compound is selected from the group consisting of growth factors, extracellular matrix molecules, proteinase inhibitors, cell adhesion molecules, angiostatic factors, apoptotic inducers, and inflammatory mediators.

21. (Previously Presented) The *in vivo* method of claim 20 wherein said compound is a growth factor.

22. (Previously Presented) The *in vivo* method of claim 21 wherein said compound is VEGF.

23. (Previously Presented) The *in vivo* method of claim 21 wherein said compound is FGF-2.

24. (Previously Presented) The *in vivo* method of claim 15 wherein said composition further comprises matrigel.

25. (Previously Presented) The *in vivo* method of claim 15 wherein said host is a SCID mouse.

26. (Previously Presented) The *in vivo* method of claim 15 wherein said compound modulates tumor angiogenesis.

27. (Currently Amended) An *in vivo* assay system for human microvasculature formation comprising:

a. A non-human, immuno-compromised host; and

b. at least one microvessel formed from a composition of microvascular endothelial cells having a recombinant expression cassette encoding telomerase, and a stably transformed genetic marker in said host, wherein host blood is transmitted through said at least one mircovessel.

28. (Previously Presented) The *in vivo* method of claim 27 wherein said host is a SCID mouse.

29. (Previously Presented) The *in vivo* method of claim 27 wherein said telomerase is a human telomerase reverse trascriptase catalytic subunit.

30. (Previously Presented) The *in vivo* method of claim 27 wherein said stably transformed genetic marker is enhanced green fluorescent protein (eGFP).

DETAILED RESPONSE TO THE OFFICE ACTION

Priority

The applicant thanks the Examiner for the reminder regarding the claim to priority. The specification has now been amended to reflect the correct claim to priority.

Specification

The Examiner has objected to the specification because Figure 6B was referred to on page 20, lines 9 and 11, but not present in the application. Figure 6B is included with this response. Support for the figure can be found at page 5, lines 7-16, and page 20, lines 9 and 11, for example. Therefore, no new matter has been added, and the Examiner is respectfully requested to withdraw the objection.

Claim Rejection-35 USC §112

Examiner had rejected claims 1-7, 9-24, 26, 27, 29, and 30 under 35 USC §112, stating that the specification enables only an *in vivo* assay system comprising a non-human host that is immune compromised. The applicant has amended the independent claims 1, 15 and 27 qualify the host as immuno-compromised. As the examiner has stated, the specification teaches how to carry out the claimed invention in SCID mice, an immuno-compromised non-human host. Hence, the amended claim are now in an allowable form, and the Examiner is respectfully requested to withdraws the rejection.

Claim Rejection-35 USC §103

Claims 1-10, 15-21, 24 and 25 have been rejected under 35 USC §103(a) as being unpatentable over Thomas (January 2000, Nature Bitotech. Vol. 18, pages 39-42) in view of Yang (1999, Jour. Biol. Chem., Vol. 274, pages 26141-26148). Additionally, claims 11, 22, 14, 22 and 26 have been rejected under 35 USC §103(a) as being unpatentable over Thomas in view of Yang, and further in view of Prewett (1999, Cancer Res. Vol. 59, pp. 5209-5218), and claims 13 and 23 have been rejected under 35 USC §103(a) as being

unpatentable over Thomas and Yang and further in view of Ueno (1197, Arter. Thromb. Vasc. Biol., Vol. 17, pp. 2453-2460).

The applicant traverses the rejection. The specification has been amended to claim the correct priority to WO 00/56898, filed March 24, 2000, which claimed priority to a US provisional application (Serial No. 60/126,015) filed March 24, 1999. Hence, the primary reference of Thomas, published in 2000, can not be used as an appropriate reference against the above mentioned claims.

Furthermore, Thomas teaches that bovine adrenocortical cells immortalized via hTERT transgene expression secrete bovine cortisone *in vivo* when transplanted into the kidney of an SCID mouse host. However, Applicant's claims are directed towards human microvascular endothelial cells form functional blood vessels *in vivo* using the same animal. The only similarities between the two are hTERT and SCID mouse. Bovine adrenocortical cells are embryologically, anatomically, functionally and evolutionarily distinct from human dermal blood microvascular endothelial cells. Because Thomas teaches how to make an hTERT-immortalized bovine cell secrete cortisone in a SCID mouse but Applicant teaches how to make hTERT-immortalized human microvascular endothelial cells form capillary blood vessels in SCID mice, Applicant's invention claimed in the above mentioned claims are not obvious from Thomas.

CONCLUSION

Withdrawal of the pending rejections and reconsideration of the claims are respectfully requested, and a notice of allowance is earnestly solicited. If the Examiner has any questions concerning this Response, the Examiner is invited to telephone Applicant's representative at (650) 335-7818.

Respectfully submitted,
G. SCOTT HERRON

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